



Europäisches Patentamt

European Patent Office

Office européen des brevets

④ Publication number:

0 231 684
A1

②

EUROPEAN PATENT APPLICATION

③ Application number: 86402709.9

④ Int. Cl. 4 G01N 30/56

③ Date of filing: 08.12.86

④ Priority: 11.12.85 US 807729

④ Applicant: LEE SCIENTIFIC, INC.

④ Date of publication of application:
12.08.87 Bulletin 87/334426 South Century Drive
Salt Lake City Utah 84123-2513(US)④ Designated Contracting States:
DE FR GB④ Inventor: Cortes, Harman J.
2417 Lambros Drive
Midland Michigan 48640(US)
Inventor: Pfeiffer, Curtis D.
5001 Dale Street
Midland Michigan 48640(US)
Inventor: Stevens, Timothy S.
5102 Foxcroft Street
Midland Michigan 48640(US)
Inventor: Richter, Bruce E.
1160 South Croff Circle
Orem Utah 84058(US)④ Representative: Paustat, Jacques et al
Cabinet Paustat 68, rue d'Hauteville
F-75010 Paris(FR)

④ Chromatography columns with cast porous plugs and methods of fabricating same.

④ Porous ceramic plugs are cast in place in chromatographic columns in order to provide supports for chromatographic beds in liquid chromatography devices and restrictors in supercritical fluid chromatographic devices. The supports are cast in place by fusing a silicate containing solution, such as one containing potassium silicate, which has been drawn into the outlet end of the column.

EP 0 231 684 A1

BEST AVAILABLE COPY

CHROMATOGRAPHY COLUMNS WITH CAST POROUS PLUGS AND METHODS OF FABRICATING SAME

The present invention relates to chromatography columns and methods of fabricating chromatography columns. More particularly, the instant invention relates to bed supports and restrictors for chromatography columns and to methods of fabricating such.

The trend in chromatography has been to move to higher pressures and smaller diameter columns for efficient solvent utilization and high column efficiency in high-performance liquid chromatography and for high column efficiency in supercritical fluid chromatography. By utilizing long chromatography columns or tubes, greater resolving power can be realized, allowing complex mixtures to be effectively separated.

Chromatography tubes having inner diameters in the range of from 10 to 5000 μm are utilized to accomplish state-of-the art chromatography. By having small inner diameters, generally not greater than about 1000 μm the volume defined by a chromatography column is minimized. Accordingly, minute samples can be analyzed with state-of-the-art chromatography columns. In order to increase the resolution of the sample components dissolved in a solvent within a chromatography column, the lengths of state-of-the-art columns are many orders of magnitude greater than the diameters thereof. For example, a chromatography column utilizing a liquid solvent has an inside diameter of 150 to 500 μm and a length of approximately 1 meter, whereas a chromatography column utilized with supercritical fluid chromatography has a length of about 20 meters and an inside diameter of approximately 50 to 150 μm .

Generally, a chromatographic column is packed with a sorbent which forms a chromatography bed. For example, the sorbent may be composed of microparticles such as C_8 bonded phase particles having outer diameters in the range of from 1 to 10 μm which are suspended in a slurry and injected under pressure into the bore of the column. During injection of the slurry and during operation of the column, one end of the column must be fitted with a plug which may be, for example, a porous plug, in order to retain the sorbent therein. According to current practices, this is accomplished by inserting a glass wool plug in the downstream end of the column in order to form a support for the bed of sorbent. This approach to plugging the outlet end of the column has not proved totally satisfactory in that it is very difficult to insert the glass wool plug in such a small opening. Moreover, since there is nothing binding the glass wool plug to the wall of the column, the plugs on occasion are ejected from the columns

due to pressure created within the columns during use thereof. This problem is addressed in United States Patent No. 4,483,773 issued November 20, 1984 to Yang, wherein alternatives to glass wool plugs are disclosed. These alternatives include utilizing narrow-bore tubing, wire, particles of a diameter larger than the constituent particles of the sorbent, and inserting a narrow-bore plug into a sleeve attached to the outside of the column. The patent to Yang clearly states that there is difficulty with the glass wool plug concept and Yang therefore resorts to a host of alternative solutions. Since the solvent in which the sample under analysis is dissolved must pass through the plug, the configuration of the plug directly affects the efficiency of the column. In part, the efficiency of the column is determined by the speed at which the solvent moves through the column and the amount of solvent which is utilized for a particular test. Generally, glass wool plugs provide high efficiency. Consequently, a desirability of any alternative to glass wool plugs should have an efficiency which at least approaches that of glass wool plugs.

In columns used for supercritical fluid chromatography (SFC) a restrictor is placed at the exit end of the chromatographic column. According to current practice, the restrictor is configured from a small-diameter capillary tube. Generally, the capillary tube forming the restrictor is butted or placed end-to-end against the chromatographic column and held in place by a union fitting or "butt-connector." Capillary tubing of Pyrex glass, fused silica and platinum iridium have been used as restrictors. The small-diameter capillary tube allows slow decompression of the mobile phase, or solvent, before detection. However, with this approach, relatively involatile solute molecules associate and condense along the walls of the small-diameter capillary tube. This results in both clogging of the opening and spiked peaks seen by the detector. In addition, laser-drilled orifices have been used as restrictors, but they are prone to blockage and breakage. Generally, these prior art restrictor designs are not entirely satisfactory in that they are separate from the columns and must be butted therewith or otherwise held in engagement therewith.

The prior art also includes a number of teachings of porous plugs used with chromatography columns. For example U.S. Patent No 3,440,864 discloses utilizing a porous stainless steel or fiber-glass disc inserted into a chromatography column. U.S. Patent No. 5,771,659 discloses a porous plug of any naturally porous or artificially porous material, such as Teflon, which is used with a

chromatographic column. U.S. Patent No. 4,142,856 discloses a disc of a microporous material formed from a polymer such as high-density polyethylene, which is inserted into a column. U.S. Patent No. 4,181,853 utilizes a porous plug of sintered steel frit which is used in a chromatography system. U.S. Patent No. 4,399,032 discloses a sintered metal terminator element having an outer rim which allegedly provides a seal with an outlet union retaining it. Each of these patents disclose arrangements of relative structural complexity wherein the plugs do not have the advantage of being "unitary" with the chromatographic column so that they do not effectively seal with the walls of the column.

U.S. Patent No. 2,723,758 discloses cast-in-place plug made of plaster of Paris which is inserted in a large-diameter support cylinder. However, the plug is not actually in a chromatographic tube since the chromatographic column of this invention does not include a tube.

In view of the aforementioned considerations, it is an object of the instant invention to provide a new and improved plug for chromatographic columns which can be used as a sorbent bed support or as a restrictor. It is a further object of the instant invention to provide new and improved processes for forming such plugs.

In particular, the invention contemplates a chromatographic column which includes a tube having a sorbent bed, an inner wall, and an inlet end and an outlet end, wherein the sorbent bed is retained within the tube by a bed support comprising a cast-in-place, ceramic plug disposed in the outlet end of the tube.

The instant invention further contemplates a chromatographic column used for supercritical fluid chromatography, having a tube containing a sorbent bed or a stationary phase coated or bonded to an inner wall of the tube and having an inlet end and outlet end, wherein the outlet end includes a restrictor which is shaped as a cast-in-place microporous ceramic plug and which is adhered to the inner wall of the tube.

The instant invention still further contemplates a process for fabricating a chromatographic column, wherein the column includes a tube of a selected material, the tube having an open end and an inner wall, wherein a microporous ceramic plug is formed in the open end by depositing a quantity of fusible material in the open end of the tube. A plug is then formed *in situ* at the end of the tube by causing the material to fuse so that the material adheres to the inner wall of the tube to form a solid microporous mass. A sorbent is then packed into the tube upstream of the plug.

In accordance with a preferred embodiment of the invention, the afore-described process is accomplished by preparing a soluble silicate solution and separating the gels therefrom. The solution is then deposited within the open end of the tube and the open end of the tube heated to fuse the solution and thereby form a plug of porous ceramic material which is integral with the open end of the tube.

Various other objects, features and attendant advantages of the present invention will become more fully appreciated as the same becomes better understood when considered in conjunction with the accompanying drawings, in which like reference characters designate the same or similar parts throughout the several views, and wherein:

Figure 1 is a perspective view of a chromatographic column which utilizes the principles of the instant invention.

Figure 2 is an enlarged cross-sectional view of the outlet end of the column of Figure 1 showing a microporous ceramic plug disposed in the outlet end and adhered to the inner wall of the column forming the tube.

Figures 3A, 3B, 3C and 3D show the steps of fabricating the end plug shown in Figure 2 wherein the outlet end of the column is immersed into a solution of fusible material, the fusible material is fused by the application of heat and a sorbent is thereafter injected into the tube.

Figure 4 is an enlarged cross-sectional view of another embodiment of the invention, wherein a microporous ceramic plug is formed in a section of capillary tube which is then abutted to the end of the chromatographic column.

Referring now to Fig. 1, there is shown a chromatographic column, designated generally by the numeral 10, which has an inlet end 11, an outlet end 12, and an intermediate portion 13 which contains a sorbent or coating on the inner wall for performing chromatographic analysis. Attached to the inlet end 11 of the chromatographic column 10 is a diagrammatically illustrated connector 15 which connects the column to the material to be analyzed, which material is dissolved or dispersed in a solvent. Connected to the outlet end 12 of the column 10 is a connector 14 for connecting the column to analytical equipment. In operation, the solvent is applied under pressure through the connector 15 so as to traverse the column 10 and exit through the outlet end 12 and the connector 14.

The column 10 is conveniently configured as a spiral because its length is usually several orders of magnitude greater than its diameter (specifically, its inner diameter). For example, if the column 10 is used for liquid chromatography, the inner diameter may be on the order of from 10 to 1000 μm , preferably from 150 to 500 μm , while the length of

the column is not critical and may be, for example, approximately 100 cm. On the other hand, if the chromatographical column 10 is used for supercritical fluid chromatography, the length of the column is not critical and may be approximately 20 meters, while the inner diameter may be from 10 to 500 μm , preferably from 50 to 150 μm . In accordance with preferred practice, the chromatographic column 10 is fabricated of fused silica material in accordance with well-known procedures and methods and has a very smooth inner wall surfaces.

Referring now to Figure 2, the outlet end 12 of tube 10 is shown greatly enlarged. Within the outlet end 12 of the tube 10, a porous ceramic plug 16 of fused material is disposed. The plug 16 is adhered to the smooth inner wall surface 17 of the tube 10 and extends back from the outlet end 11 of the tube a distance "L" which varies in accordance with the purpose for which the plug is used. For example, if the plug 16 is used in a tube 10 that is part of a supercritical fluid chromatography system, the distance "L" might be 0.5 mm to 2 cm. If the plug 16 is being used for a liquid chromatography system, the distance "L" might be 0.5-3.0 mm. The selection of the distance "L" is also dependent on the particular inner diameter of the tube "D".

Disposed behind the porous ceramic plug 16 is sorbent bed 18, which is normally injected into the tube 10, or a liquid stationary phase coated or bonded to the inner wall subsequent to forming the plug. Since the plug is porous, a suspension of sorbent 18 can be easily injected into the tube 10.

Referring now to Figures 3A to 3D, there is shown a preferred method for forming the plug 16. A solution 20a containing, for example, potassium silicate, such as that known as Kasil™ Number 1, is provided. The solution is centrifuged to remove gels and the end 12 of the chromatographic column 10 is simply immersed therein as shown in Figure 3b. A portion 20b of the solution is drawn up into the tube 10 by capillary action or introduced with, for example, a syringe. As shown in Figure 3c, the end 12 of the tube 10 with the fusible silicate solution 20b is then heated by conventional means, such as a steam bath 21, in order to fuse the solution 20b into the solid porous ceramic plug 16, while adhering the material of the plug 16 to the inner wall 17 of the tube 10. Thereafter, the sorbent bed material 18 is packed into the tube 10.

The plug 16 may be used for two different purposes. If the chromatographic column 10 is being used for liquid chromatography, then the plug 16 serves as a support for the sorbent bed 18 so as to retain the sorbent bed 18 in the column both during packing of the sorbent bed into the column and during use of the column. The plug 16 withstands pressures applied to the inlet 11 end of

the column 10 in excess of 8,000 psi while having a chromatographic efficiency similar to the chromatographic efficiency of the glass wool plugs of the prior art.

The plug 16 may also be used as a restrictor in the outlet end of a chromatography tube 10 used for supercritical fluid chromatography. In this embodiment of the invention, it has been found that a plug 16 used as a restrictor minimizes the distance over which decompression of the supercritical fluid solvent occurs while increasing drastically the number of paths through the restrictor that the solvent may travel. Accordingly, molecular association and condensation is minimized and at best totally eliminated. Consequently, line clogging is avoided as well as detector "spiking". In addition, the plug 16 does not cause band spreading. The case *in situ*, or cast-in-place, porous ceramic plug 16 is of special interest in reducing spilling which occurs with higher molecular weight samples and in reducing the exit clogging which also occurs with high molecular weight samples. While a restrictor 16 is shown in Figure 2 which is cast in place directly to the chromatographic tube 10, the restrictor may be formed on a separate portion of silica capillary tube 22 and the separate portion coupled to the outlet end 12 of the chromatographic tube 10 with a coupling 23.

While the plug 16 shown in the drawings and discussed thus far herein extends completely across the cross-section of the outlet end 12 of the tube 10, it is within the scope of the invention to interrupt this extension by incorporating fibers, hollow tubes and the like within the plug.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. In the following examples, all temperatures are set forth uncorrected in degrees Celsius; unless otherwise indicated, all parts and percentages are by weight.

Example 1

A support bed or support structure for supporting sorbent within a fused silica liquid chromatographic column having an internal diameter of 250 μm and a length of 99 cm was prepared by immersing the outlet end of the column in a solution of potassium silicate, removing the outlet end from the potassium silicate and heating the outlet end in a steam bath for approximately one hour to cause polymerization of the potassium silicate solu-

tion. The potassium silicate solution was a solution of Kasil™ Number 1 having a weight ratio of silicon dioxide to water of 2.50 and a density of 28.80° Bé (Baumé) to which formamide was added in a ratio of 85 percent Kasil Number 1 to 15 percent formamide. Before immersing the outlet end of the chromatographic column in the solution, the solution was centrifuged to precipitate gels.

After the porous ceramic plug, according to the instant invention, was formed in the outlet end of the chromatographic tube in order to form a support for the sorbent, a pressure of 8,000 psi was supplied to the inlet end of the column in order to test the integrity of the plug and the adherence of the plug material to the very smooth interior surface of the chromatographic tube.

The chromatographic tube was then packed with ZORBAX® ODS, 7 μm particle size (DuPont, Wilmington, DE, USA) and tested. In this initial test, the length of the plug forming the support was approximately 4 cm. The resulting chromatogram indicated very poor efficiency, much lower than that obtained by using the prior art glass wool approach.

Example 2

All of the steps of Example 1 were repeated with the exception of reducing the length of the plug to 1 mm. Upon filling the chromatographic tube with sorbent and testing the tube, very good results were attained and efficiencies comparable to using a glass wool plug, but without the drawbacks of using glass wool plugs.

Example 3

A chromatographic column used in supercritical fluid chromatography was provided with a porous ceramic plug for use as a restrictor in the outlet end of the column. As with examples 1 and 2, a solution Kasil™ Number 1 and formamide was prepared in a ratio of 85 percent Kasil Number 1 to 15 percent formamide. The solution was centrifuged to precipitate the gels. A portion of fused silica capillary material having a length of about 2 cm and an internal diameter of 80 μm was immersed into the solution and a plug cast therein by heating the capillary material for about 1 hour in a steam bath. The capillary material was then connected to the end of an analytical chromatographic column having an internal diameter of 80 μm, a length of 10 meters and a film of polysiloxane stationary phase having a thickness of 0.25 μm bonded to the inner surface of the tube. The column was tested by running high molecular weight hydrocarbons -

(paraffin wax) therethrough. In the resulting test, no spiking occurred and there was no band spreading attributable to the fused, microporous plug. Moreover, there was no clogging. The length of the microporous plug in this particular example was about 2 cm long. The sample analyzed was a mixture of C₆, C₈, C₁₀, C₁₂, C₁₄, and C₁₆ n-alkanes.

5 The preceding examples can be repeated with similar success by substituting the generically or specifically described reactants and/or operating conditions of this invention for those used in the preceding examples.

10 From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions.

15 20 Claims

1. A tube for retaining a selected material within the tube comprising:
- 25 a plug disposed within the interior of the tube, said plug being made of a microporous material and chemically fused to the interior wall of said tube.
2. The tube of Claim 1, wherein the tube is a chromatographic column having an inner diameter of from 10 to 1000 μm.
3. The tube of Claim 1 or 2, wherein said plug extends uninterrupted completely across the interior diameter of the tube.
- 35 4. The tube of Claim 1 or 2, wherein the plug extending across the interior diameter of the tube is interrupted by at least one object disposed within the plug.
5. The tube of Claim 1, wherein said microporous material is prepared from a soluble silicate solution.
- 40 6. The tube of Claim 5, wherein said silicate solution is potassium silicate.
7. The tube of Claim 1, wherein said tube is attached to a chromatographic column.
- 45 8. A chromatographic column used for supercritical fluid chromatography, a tube having an inner wall and containing a chromatographic bed or a liquid stationary phase coated or bonded to the inner wall, an inlet end and an outlet end, the outlet end including a restrictor which restrictor allows controlled expansion of a supercritical fluid; the restrictor being configured as a plug of microporous ceramic material which has been cast in place and which is chemically adhered to the inner wall of the tube, whereby a multitude of paths are provided for solutes to exit from the column, the
- 50
- 55

distance over which decompression occurs is controlled and molecular association and condensation is minimized within the plug.

9. The chromatographic column of Claim 8, wherein the tube has an inner diameter in the range of about 10 μm to about 500 μm .

10. The chromatographic column of Claim 9, wherein the tube has an inner diameter of from 50 to 150 μm .

11. The chromatographic column of Claim 8, 9 or 10 wherein the restrictor has a length of from 0.5 to 2 cm.

12. A chromatographic column comprising a tube containing a chromatographic bed and having an inner wall, an inlet end and an outlet end, a bed support positioned at the outlet end, for supporting the chromatographic bed; the bed support being a plug of porous ceramic material cast *in situ* at the outlet end and adhered to the inner wall of the tube.

13. The chromatographic column of Claim 12, wherein the inner diameter of the tube is in the range of about 10 μm to about 1000 μm .

14. The chromatographic column of Claim 13, wherein the inner diameter of the tube is from 100 to 500 μm and the length of the bed support is in the range of from 0.50 mm to 3.0 mm.

15. A process for fabricating a chromatographic column wherein the column includes a tube of a selected material, the tube having an open end and an inner wall, the process comprising the steps of:

(a) providing a fusible material which is microporous upon fusing and which adheres to the material of the tube upon fusing;

(b) depositing a quantity of the fusible material in at least one open end of the tube;

(c) forming a plug *in situ* by fusing the material within the open end of the tube and adhering the material to the inner wall of the tube to form a solid microporous mass; and

(d) filling the tube with a sorbent to form a chromatographic bed which bed is retained within the tube inboard of the plug, or coating or bonding the inner wall of the tube with a liquid stationary phase.

16. The process of Claim 15, wherein the fusible material is a heat fusible material and wherein the step of forming the plug *in situ* includes heating the material.

17. The process of Claim 16, wherein the solution further includes formamide mixed with the silicate.

18. The process of Claim 16, wherein the silicate is potassium silicate.

19. The process of Claim 15, wherein the step of depositing the fusible material in at least said one open end of the tube comprises immersing the open end of the tube in the fusible material and allowing the material to be drawn into the tube.

20. The process of Claim 15, wherein the tube is a small diameter tube having an inner diameter in the range of from 10 μm to 1000 μm .

21. The process of Claim 20, wherein the tube has an inner diameter of from 150 to 500 μm .

22. The process of Claim 15, wherein the chromatographic column is used for supercritical fluid chromatography and wherein the plug is disposed in the tube and the plug forms a microporous restrictor restricting the flow within the tube.

23. The process of Claim 22, wherein the tube has an inner diameter in the range of from 10 μm to 500 μm .

24. The process of Claim 23, wherein the tube has an inner diameter of from 50 to 150 μm .

D 231 684

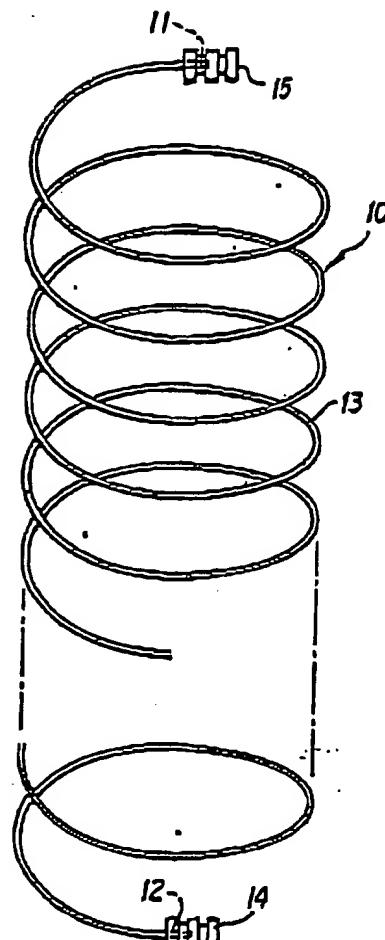


FIG. 1

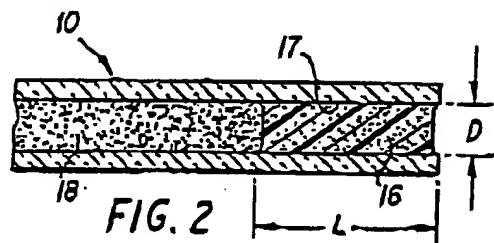


FIG. 2

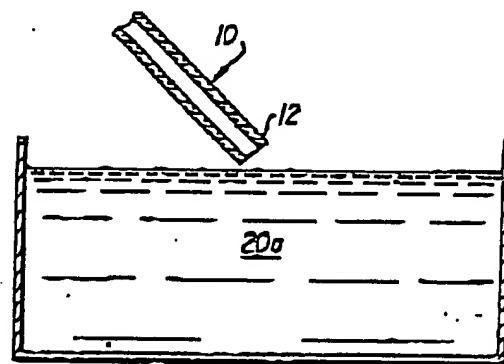


FIG. 3A

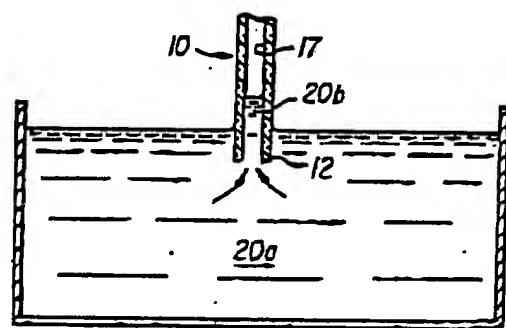


FIG. 3B

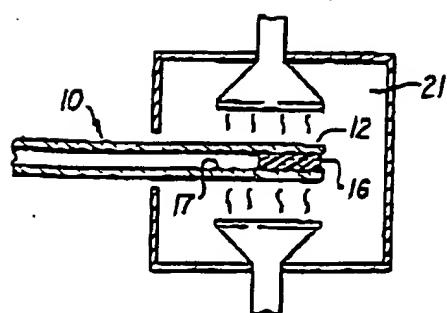


FIG. 3C

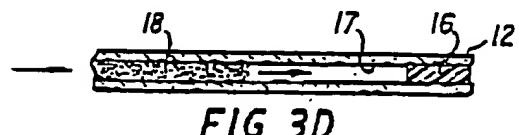


FIG. 3D

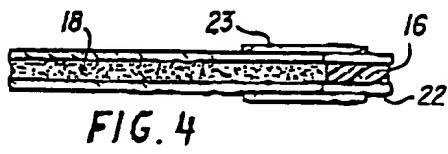


FIG. 4



European Patent
Office

EUROPEAN SEARCH REPORT

Application number

EP 86 40 2709

DOCUMENTS CONSIDERED TO BE RELEVANT

DOCUMENTS CONSIDERED TO BE RELEVANT		Relevant to claim	CLASSIFICATION OF THE APPLICATION (in. Cl.4)
Category	Citation of document with indication, where appropriate, of relevant passages		
D, Y	GB-A-2 128 099 (VARIAN ASSOCIATES) * Abstract; page 2, lines 38-57; page 6 *	1-3, 8-10, 12-13	G 01 N 30/56
Y	US-A-3 692 569 (A.J. BAUMAN) * Column 2, lines 38-56 - column 5 *	1, 3, 12-15, 18	
A	US-A-2 733 135 (W.B. HUCKABAY) * Column 5, lines 1-31 *	1	
A	US-A-3 250 395 (H.K. BLUME) -----		
		TECHNICAL FIELDS SEARCHED (in. Cl.4)	
		G 01 N 30/56 G 01 N 30/50	

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.